

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
22 January 2009 (22.01.2009)

PCT

(10) International Publication Number
WO 2009/011871 A3

(51) International Patent Classification:

C07D 471/02 (2006.01) A61K 31/433 (2006.01)
C07D 285/135 (2006.01) A61P 35/00 (2006.01)
C07D 285/125 (2006.01) A61P 29/00 (2006.01)

(21) International Application Number:

PCT/US2008/008690

(22) International Filing Date: 15 July 2008 (15.07.2008)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:

60/959,974 17 July 2007 (17.07.2007) US

(71) Applicant (for all designated States except US): AMGEN INC. [US/US]; One Amgen Center Drive, Patent Operations M/S 28-2-C, Thousand Oaks, CA 91320-1799 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): ALLEN, John, G. [US/US]; 5255 Via Capote, Newbury Park, CA 91320 (US). BOURBEAU, Matthew, P. [US/US]; 22038 Vanowen Street, Unit 106, Woodland Hills, CA 91303 (US). DOMINGUEZ, Celia [US/US]; 8606 Allenwood Road, Los Angeles, CA 90046 (US). FOTSCH, Christopher, H. [US/US]; 533 Timberwood Avenue, Thousand Oaks, CA 91360 (US). HAN, Nianhe [US/US]; 4522

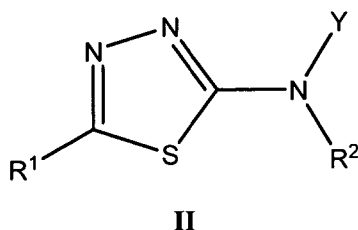
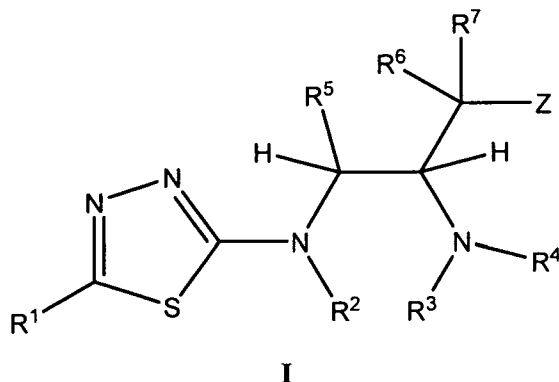
Via Laguna, Thousand Oaks, CA 91320 (US). HONG, Fang-tsao [—/US]; 822 Lynnmere Drive, Thousand Oaks, CA 91360 (US). HUANG, Xin [US/US]; 138 Aldrich Street, Roslindale, MA 02131 (US). LEE, Matthew, R. [US/US]; 4416 Park Mallorca, Calabasas, CA 91302 (US). LIU, Qingyian [CN/US]; 4631 Paseo Girasol, Camarillo, CA 93012 (US). REICHELT, Andreas [DE/US]; 6625 Pinnacle Way, Moorpark, CA 93021 (US). TADESSE, Seifu [US/US]; 130 Marblehead Street, Simi Valley, CA 93065 (US). WANG, Xianghong [US/US]; 11621 Country Springs Court, Moorpark, CA 93021 (US). YAO, Guomin [CN/US]; 2092 W. Hillcrest Drive, Apt. #C102, Newbury Park, CA 91320 (US). YUAN, Chester Chenguang [US/US]; 1416 Geyser Court, Newbury Park, CA 91320 (US). ZENG, Qingping [US/US]; 4831 Via Camino, Thousand Oaks, CA 91320 (US).

(74) Agent: FRIEDRICHSEN, Bernard, P.; One Amgen Center Drive, Patent Operations, M/S 28-2-C, Thousand Oaks, CA 91320-1799 (US).

(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM, AO, AT, AU, AZ, BA, BB, BG, BH, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KN, KP, KR, KZ, LA, LC, LK,

[Continued on next page]

(54) Title: THIADIAZOLE MODULATORS OF PKB



(57) Abstract: The invention relates to thiazole compounds of Formula I and Formula II and compositions thereof useful for treating diseases mediated by protein kinase B (PKB) where the variables have the definitions provided herein. The invention also relates to the therapeutic use of such thiazole compounds and compositions thereof in treating disease states associated with abnormal cell growth, cancer, inflammation, and metabolic disorders.

WO 2009/011871 A3



LR, LS, LT, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RS, RU, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (*unless otherwise indicated, for every kind of regional protection available*): ARIPO (BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MT, NL, NO, PL, PT, RO, SE, SI, SK, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Declaration under Rule 4.17:

— *as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))*

Published:

— *with international search report*
— *before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments*
— *with sequence listing part of description published separately in electronic form and available upon request from the International Bureau*

(88) Date of publication of the international search report:

30 April 2009

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/008690

A. CLASSIFICATION OF SUBJECT MATTER
 INV. C07D471/02 C07D285/135 C07D285/125 A61K31/433 A61P35/00
 A61P29/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED
 Minimum documentation searched (classification system followed by classification symbols)
 C07D A61P A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
 EPO-Internal, EMBASE, WPI Data, BEILSTEIN Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2006/044860 A (AMGEN INC [US]; ZENG QINGPING [US]; YAO GUOMIN [US]; WOHLHIETER GEORGE) 27 April 2006 (2006-04-27) cited in the application the whole document claim 1; examples 3,20,22,101,176-178	1-64, 66-138, 140-200, 202-237
X	MISHRA L ET AL: "Synthesis and fungicidal activity of some 5-membered heterocyclic derivatives containing benzimidazoles." BIOSCIENCE, BIOTECHNOLOGY, AND BIOCHEMISTRY JUN 1993, vol. 57, no. 6, June 1993 (1993-06), pages 989-991, XP002497950 ISSN: 0916-8451 compounds 8-12	91

Further documents are listed in the continuation of Box C.

See patent family annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *Z* document member of the same patent family

Date of the actual completion of the international search 13 October 2008	Date of mailing of the international search report 03/03/2009
--	--

Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3016	Authorized officer Skulj, Primoz
--	---

INTERNATIONAL SEARCH REPORT

International application No
PCT/US2008/008690

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	ZHURAVEL' I O ET AL: "Synthesis of substituted 3-(5-amino-[1,3,4]thiadiazol-2-yl)-2H-pyridino [2,3- c]pyridin-2-ones" JOURNAL OF HETEROCYCLIC CHEMISTRY 200407 US, vol. 41, no. 4, July 2004 (2004-07), pages 517-524, XP002497951 ISSN: 0022-152X	
A	WO 2004/056789 A (WARNER LAMBERT CO [US]; BIWERSI CATHLIN MARIE [US]; WARMUS JOSEPH SCOT) 8 July 2004 (2004-07-08)	
X,P	WO 2008/036308 A (SIGNAL PHARMACEUTICALS LLC [US]; D SIDOCKY NEIL R [US]; HARRIS ROY L I) 27 March 2008 (2008-03-27) cited in the application the whole document	1

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US2008/008690

Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. As all required additional search fees were timely paid by the applicant, this international search report covers allsearchable claims.
2. As all searchable claims could be searched without effort justifying an additional fees, this Authority did not invite payment of additional fees.
3. As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see annex

Remark on Protest

- The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. claims: Parts of claims 1-64, 66-138, 140-200, 202-237
Compounds of Formula I, IV, V where R5 is H

2. claims: Parts of 1-237
Compounds of Formula I, IV, V where R5 is not H

3. claims: Parts of claims 91-95, 99-187
Compounds of formula IV (see detail below)

4. claims: Parts of claims 91-95, 99, 100, 103-129, 181-187
Compounds of formula IV (see detail below)

5. claims: Parts of claims 91-95, 99, 100, 103-129, 181-187
Compounds of formula IV (see detail below)

6. claims: Parts of claims 91-95, 99, 100, 103-129, 181-187
Compounds of formula IV (see detail below)

7. claims: Parts of claims 91-187
Compounds of formula IV (see detail below)

8. claims: Parts of claims 1-237
Any subject matter not covered above

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No PCT/US2008/008690

Patent document cited in search report	A	Publication date		Patent family member(s)	Publication date
WO 2006044860	A	27-04-2006		AU 2005295441 A1	27-04-2006
				BR PI0516609 A	29-04-2008
				CA 2583217 A1	27-04-2006
				EP 1809282 A2	25-07-2007
				JP 2008516986 T	22-05-2008
				KR 20070073791 A	10-07-2007
				US 2008255145 A1	16-10-2008
				US 2008269243 A1	30-10-2008
				US 2006154961 A1	13-07-2006
<hr style="border-top: 1px dashed black;"/>					
WO 2004056789	A	08-07-2004		AU 2003286306 A1	14-07-2004
				BR 0317254 A	01-11-2005
				CA 2509405 A1	08-07-2004
				EP 1578736 A1	28-09-2005
				JP 2006516967 T	13-07-2006
				MX PA05006803 A	08-09-2005
<hr style="border-top: 1px dashed black;"/>					
WO 2008036308	A	27-03-2008		US 2008242694 A1	02-10-2008